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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,200	11/18/2003	Manne Satyanarayana Reddy	BULK 3.0-032	4125

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EXAMINER	
MORRIS, PATRICIA L	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 04/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,200	REDDY ET AL.	
	Examiner	Art Unit	
	Patricia L. Morris	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9,11-17 and 19-34* is/are pending in the application.

4a) Of the above claim(s) *19-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-9,11-17,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-9, 11-17, 33 and 34 are under consideration in this application.

Claims 19-32 remain held withdrawn from consideration as being drawn to nonelected subject matter 37 CFR 1.142(b).

Election/Restrictions

The restriction requirement is deemed sound and proper and is hereby made FINAL.

This application contains claims 19-32 drawn to an invention nonelected with traverse in the reply filed July 19, 2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-9, 11-17, 33 and 34 are rejected under 35 U.S.C. 102(a) and/or (e) as being anticpated by Cotton et al. for the reasons set forth in the previous Office action.

Again, Cotton et al. specifically disclose the instant compound. Note, example 1, therein. Also, note column 2, line 47-50, wherein it is recited that magnesium S-omeprazole hydrates are highly crystalline. Hence, the instant compound is deemed anticipated therefrom.

Applicants appear to couch their arguments for the process of making the compound. Applicants are claiming the **compound and not the processes of making.**

Contra to applicants' arguments in the instant response, a novel chemical product is identified first by its "chemical nature", i.e, elemental and atom content. It is a well known fact that many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the miolecules in the crystal lattice (see US Pharmacopia). Thus *in the strictest sense, polymorphs are different crystalline forms of the* ***same pure substance*** *in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 1-2).

Claim Rejections - 35 USC ∋ 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-9, 11-17, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over d Cotton et al. in view of Bohlin et al., Lindberg et al., Haleblian et al., Muzaffar et al., Chemical & Engineering News, Feb. 2003, US Pharmacopia, and Concise Encyclopedia Chemistry, pages 872-873 (1993).

Again, Cotton et al, teach the crystalline form of the magnesium salt of s-omeprazole trihydrate. Note example 1 therein. Bohlin et al. and Lindberg et al. teach that s-omeprazole and its salts can exist in different crystalline states. Muzaffar et al. and Haleblian et al. teach that compounds can exist in amorphous forms as well as in crystalline forms. Note, for example, column 1, lines 58-63, of Bohlin et al. or page 60 of Muzaffar et al. Chemical & Engineering News, US Pharmacopia and Concise Encyclopedia teach that at any particular temperature and pressure, only one crystalline form is thermodynamically stable. Hence the claimed crystalline form as well as its relative selectivity of properties *vis-a-vis* the known compound are suggested by the references. It would appear obvious to one skilled in the art in view of the references that the instant compound would exist in different crystalline forms. No unexpected or unobvious properties are noted.

Contra to applicants' assertions in the instant response, one having ordinary skill in the art would find the claims prima facie obvious because the instant claims differ from the known product merely by forms and the physical properties innate to the forms. It is well recognized in

the pharmaceutical field that many solids exhibit polymorphism which is the innate nature of the particular drug. See US Pharmacopia. It is also well recognized in the art that the different polymorphs will display different physical properties such as X-ray diffraction, melting point, etc. (see page 911 of Haleblian or page 33 of Chemical Engineering News). As clearly stated by Brittain (p.1-2) supra, as well as set forth by the court in In re Cofer 148 USPQ 268, ex parte Hartop 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable. The instant compounds are drawn to the ***same pure substance*** as the prior art that only have *different arrangements and/or different conformations of the molecule.* A mere difference in physical property is a well known conventional variation for the same pure substance is prima facie obvious. The instant compounds are not new as asserted by applicants.

Applicants do not point to any objective evidence which demonstrates that the claimed compounds as a class exhibit any properties which are actually different from the closest prior compounds embraced by Muller et al. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977); In re Hoch, 428 F.2d 1341, 166 USPQ 406 (CCPA 1970). Further, applicants have failed to show that the instant compound *vis-à-vis* the prior art compound shows any unexpected or superior properties in reducing gastric secretion.

Claim Rejections - 35 USC ∋ 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-9, 11-17, 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Again, there is a lack of description as to whether the compositions are able to maintain the compound in the cyrstalline form claimed. Processing a compound into a pharmaceutical composition could create a different form than the crystalline form being claimed or even back to the compound itself. See pages 912-913 of Habeblian. Doelker et al. Abstract, "One may also observe changes in technology or pharmaceutical properties that are due to polymorphic environmental conditions undergone by the product or dosage form." Taday et al. p 831...Once in the desired crystalline form, the polymorphic form may be changed by incorrect storage or even during tablet preparation" and p. 836, figure 8, wherein the compound form four in the pharmaceutical composition resulted in similar spectra. The specification fails to describe the pharmaceutical compositions claimed in terms of their X-ray diffraction pattern or infrared spectrum data. The X-ray diffraction and Infrared spectrum data in the specification only pertains to the magenesium hydrate rather than the compositions being claimed.

Contra to applicants' arguments in the instant response, applicants have **failed to provide any objective evidence that the instant polymorphs are indeed maintained in the compositions.** Chemical & Engineering News disclose that formulation of drugs or pharmaceuticals in its metastable forms, for example, on polymorph, is highly unpredictable. The metastable forms will disappear and change into the most thermodynamically stable form.

Muzaffar et al., p. 60 states "At any one temperature and pressure only one crystal form of a drug is stable and any other polymorph existing under these conditions will convert to the stable form." And p. 63-65 (a)-(h) pharmaceutical preparing processes affect polymorphism.

The specification lacks description of how the pharmaceutical compositions can be prepared in order to maintain the particular compound of a particular form with the particular infrared spectra and X-ray diffraction being claimed. Otsuka et al., p. 852 "..in formulation studies and the method preparing CBZ has been shown to affect the drug's pharmaceutical properties through the polymorphic phase transformation of the bulk CBZ powder during the manufacturing process." Disclosure of X-ray diffraction patterns for pharmaceutical compositions comprising the crystalline forms are lacking in the specification. The X-ray diffraction patterns in figure 1 and infrared spectra only supports the crystalline form of magnesium esomperazole trihydrate.

Applicants' assertions and allegations in the instant response do not take the place of objective evidence. Applicants have failed to show that the polymorph in the composition will maintain its form after pharmaceutical formulation. Applicants have provided no objective evidence that the instant polymorphs will not be identical to prior art compound because *"when a crystalline solid is dissolved in solvent, the crystalline structure is lost so that different polymorphs of the same substance will show the same absorption spectra as solution"* (see Jain p.316). It is well known that the compound will become amorphous in solution. It is well recognized in the art that for a given crystalline form of a drug, *in absence of explicit* enabling description, in view of the high degree of unpredictability, even if one is in possession of a

particular crystalline form, no predictability can be found that such forms will prevail in pharmaceutical compositions. See Chemical & Engineering News.

Further, the specification has also not described how all the crystalline forms and compositions being claimed will be maintained and prevented from converting to other forms when used in the treatment of disorders associated therewith with gastric acid secretion. In addition, it is well recognized in the art that the compound is given to the subject in a physicological environment, *i.e.,* administered. As discussed supra, there is no description or enabling support that the instant polymorph will be in its physical and biological activity results from the particular form instead of the solution state of the compound.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention

The nature of the invention is the preparation of novel crystalline forms of the instant salt and compositions and for treating disorders associated with gastric acid secretion.

State of the Prior Art

Polymorphs arise when molecules of a compound stack in the solid state in distinct ways. (See Chemical Engineering News, page 32). Although identical in chemical composition, crystalline hydrates can have very different properties. They are distinguishable by various analytical techniques, especially X-ray powder diffraction. Additionally, hydrates may dehydrate. Hydrates tend to convert from less stable to more stable forms. No method exists to predict the polymorphs of a solid compound with any significant certainty. In drug design, it is best to work with the most stable polymorph, because it will not convert any further, however, the most stable polymorph usually is the least soluble. To improve bioavailability, drug companies sometimes trade off polymorph stability with solubility, choosing to work instead with the less stable forms first, also known as the metastable forms. Polymorphs can convert from one form to another during the manufacturing process of a pharmaceutical drug. See Chemical Engineering News, page 33. This is why it is important to monitor the polymorph during manufacture of the drug to see if it persists during manufacture.

The amount of direction or guidance and the presence or absence of working examples

Figure 1 of the specification only disclose the X-ray diffraction pattern of one compound, i.e., magnesium esomeprazole trihydrate in the crystalline form rather than the compositions being claimed in terms of the specific X-ray diffraction patterns. Hydrates often change into other forms during drug manufacture into a pharmaceutical composition. Based on the

unpredictability in the art, the applicant is not entitled to the X-ray diffraction patterns claimed for the compositions and pharmaceutical compositions.

Further, the specification fails to show that the instant hydrates treat any gastroinstestinal disorder such as ulcers by reducing gastric secretion. As evidenced by the art of record, it is well known that hydrates can convert to the original compound.

The breadth of the claims

The breadth of the claims are drawn to the specific crystalline form and in addition to the compositions and pharmaceutical compositions and the method of reducing gastric acid secretion for the treatment of all unknown disorders associated therewith.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the pharmaceuticals compositions being claimed and verifying that they have the specific X-ray diffraction patterns being claimed which are not disclosed in the specification. There is also lack of guidance as to whether the instant hydrate rather than the original compound treats any gastrointestinal disorder complication associated with gastric acid secretion.

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6-9, 13-17, 33 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Again, claims 1 and 18(previous claim 33) are drawn to the same scope; In re Thorpe, 227 USPQ 964. Claim 1 demonstrates that applicants are able to describe the instant hydrates here without resorting to the process. Accordingly, claim 18 is improper here. Product-by-process claims are not proper in the same application where it has been demonstrated that the compound in question may be described by means of a chemical structure; In re Hughes, 182 USPQ 106 (CCPA 1974). Applicants merely assert that the rejection be withdrawn. The rejection will not be withdrawn for the reasons clearly stated.

Again, claims 1, 6-9, 13-17, 33 and 34 contains the trade name esomeprazole. Where a trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trade name is used to identify/describe a structure of a chemical compound and, accordingly, the identification/description is indefinite.

Applicants allege that esomeprazole is not a trade name. The name certainly does **not define the chemical name of the compound. Only the IUPAC name is the correct name of the compound.** The rejection will **not** be withdrawn.

The claims measure the invention. United Carbon Co. V. Binney & Smith Co., 55 USPQ 381 at 384, col. 1, end of 1st paragraph, Supreme Court of the United States (1942).

The U.S. Court of Claims held to this standard in Lockheed Aircraft Corp. v. United States, 193 USPQ 449, AClaims measure invention and resolution of invention must be based on what is claimed.

The C.C.P.A. in 1978 held a that invention is the subject matter defined by the claims submitted by the applicant. We have consistently held that no applicant should have limitations of the specification read into a claim where no express statement of the limitation is included in the claim. In re Priest, 199 USPQ 11, at 15.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

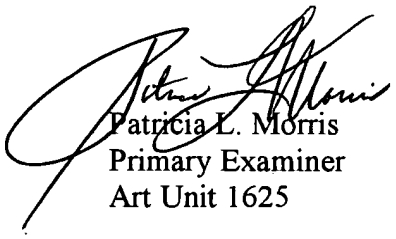
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Patricia L. Morris
Primary Examiner
Art Unit 1625

plm
April 4, 2006